with those who maintained a normal temperature (ie, >36°C). Greater degrees of hypothermia (ie, <34°C vs ≥34°C) did not result in more benefit. The strength of our analysis was the large number of subjects in the database. Additional examination of the data is indicated to better identify the breakpoint temperature at which benefit will be derived.

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EDITORIAL COMMENTARY

To cool or not to cool?

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See related article on pages 2712-8.

To cool or not to cool—that is the question that is raised by the recent study by Greason and colleagues[1] appearing in this issue of the *Journal*. Greason and colleagues[1] used the Society of Thoracic Surgeons database to evaluate patients undergoing nonemergency on-pump isolated coronary artery bypass grafting (CABG) with specific attention to the effect of lowest intraoperative recorded core body temperature on the primary end point of operative mortality and secondary end points of stroke, reoperation for bleeding, and a combined infection end point.

The main strength of the study is in the large number of patients included in the analysis (N = 142,541), because previous studies have had too few patients to demonstrate meaningful statistical differences between groups. Patients were categorized into temperature groups according to the lowest recorded intraoperative temperature: moderate hypothermia (≤34°C; N = 94,777), mild hypothermia (>34°C and ≤36°C; N = 42,750), and normothermia (>36°C; N = 5014). The study spanned an 18-month period.

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Univariate analysis demonstrated that mild hypothermia was better than moderate hypothermia which in turn was better than normothermia for the end point of operative mortality; however, operative mortality was 1.5% in the moderate hypothermia group, 1.3% in the mild hypothermia group, and 2.1% in the normothermia group. After multivariate analysis, mild and moderate hypothermia were protective relative to normothermia for the primary end point of operative mortality; however, mild hypothermia was not protective relative to moderate hypothermia.

Unfortunately, this large study was retrospective in nature and involved very different populations and enrollment biases. Clearly, the normothermic group was the sickest of all groups; it had more patients with lower ejection fraction, diabetes mellitus, chronic lung disease, recent myocardial infarction, unstable angina, higher New York Heart Association classification, atrial fibrillation or flutter, and urgent status. The normothermic patient group also had a higher incidence of readmission to the intensive care unit. In addition, Greason and colleagues[1] excluded patients with known predictors of operative mortality (N = 73,780), including reoperation, shock, emergency status with resuscitation, or salvage, to "create study cohorts that were as homogeneous as possible." This may have introduced additional bias, despite multivariate adjustment attempts.

Do the results of this study indicate that hypothermia is good, hyperthermia is bad, or both? Greason and colleagues[1] speculated that hypothermia is protective as a result of reduced oxygen demand during CABG; however, does this really affect operative mortality? Hypothermia may also be detrimental because it is known to be associated

with coagulopathy, altered oxygenator performance, prolonged emergence from anesthesia, and delayed drug metabolism after surgery.[2,3] Interestingly, the moderate hypothermia group in the study of Greason and colleagues[1] had a higher incidence of intraoperative and postoperative blood transfusion, probably related to coagulopathy. Conversely, hyperthermia is known to be associated with increased risk of mediastinitis, altered cerebral oxygen transfer, and, more importantly, acute kidney injury, which is known predictor of poor outcome after CABG.[4-7] It is not possible to determine whether this had a role in the observed differences in operative mortality, because all postoperative complications, including the incidence of acute kidney injury, were not reported by Greason and colleagues.[1]

The results of the Greason study prompt the question, "Will cooling my patient just 1°C more on pump reduce my CABG operative mortality rate? If so, how low do I go?" We as surgeons intuitively assume that reduced oxygen consumption (systemic and myocardial) is good—we anecdotally "drift" on bypass to a certain temperature and then often cool additional degrees to "protect the patient and myocardium" if a case becomes more complicated and lengthy intraoperatively. Knowing whether these maneuvers are truly beneficial would be of practical benefit to patient outcomes. Similarly, these maneuvers could be easily achieved as we maintain complete control over patient temperature during on-pump CABG.

To date, a few small randomized studies have concluded that neurologic injury, leukodepletion, and the release of inflammatory mediators during cardiopulmonary bypass are independent of temperature.[8-10] The study by Greason and colleagues[1] thus brings to light an important topic for a large prospective, randomized trial of intraoperative temperature regulation with assessment of inflammatory mediators, organ injury markers, and long-term outcomes (including cause of death) after on-pump CABG. Until such a trial is conducted, the clinical implications of the reported findings remain unknown.

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